

This Page Is Inserted by IFW Operations
and is not a part of the Official Record

BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

**As rescanning documents *will not* correct images,
please do not report the images to the
Image Problem Mailbox.**



1/34

RECEIVED
FEB 14 2003
TECH CENTER 1000-10

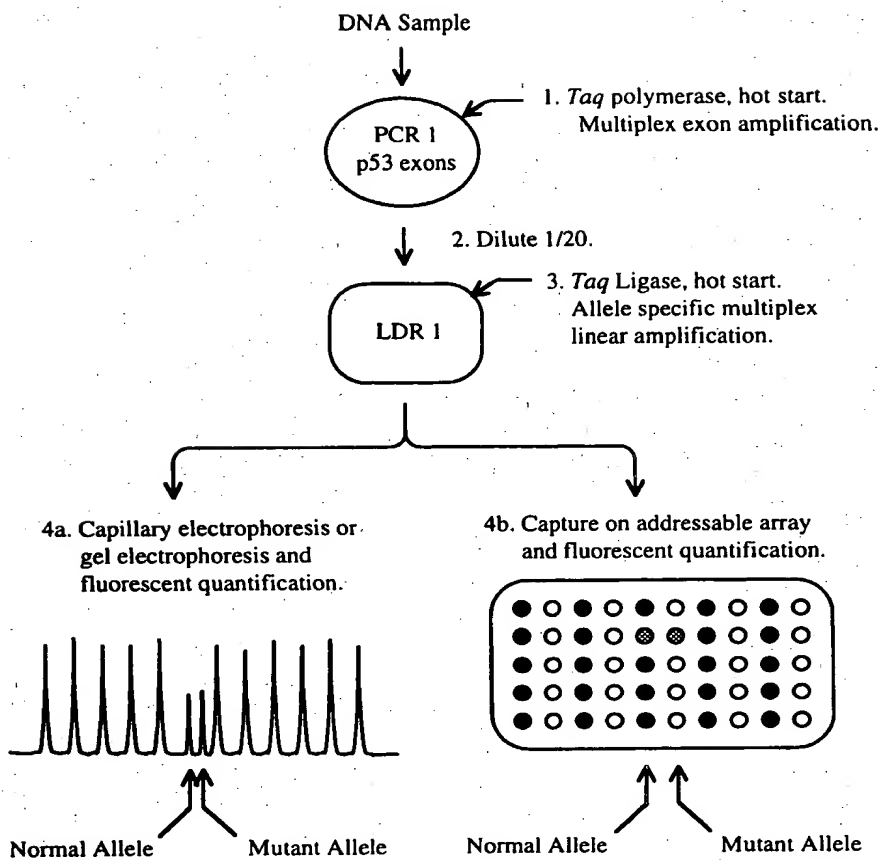


FIG. 1

2/34

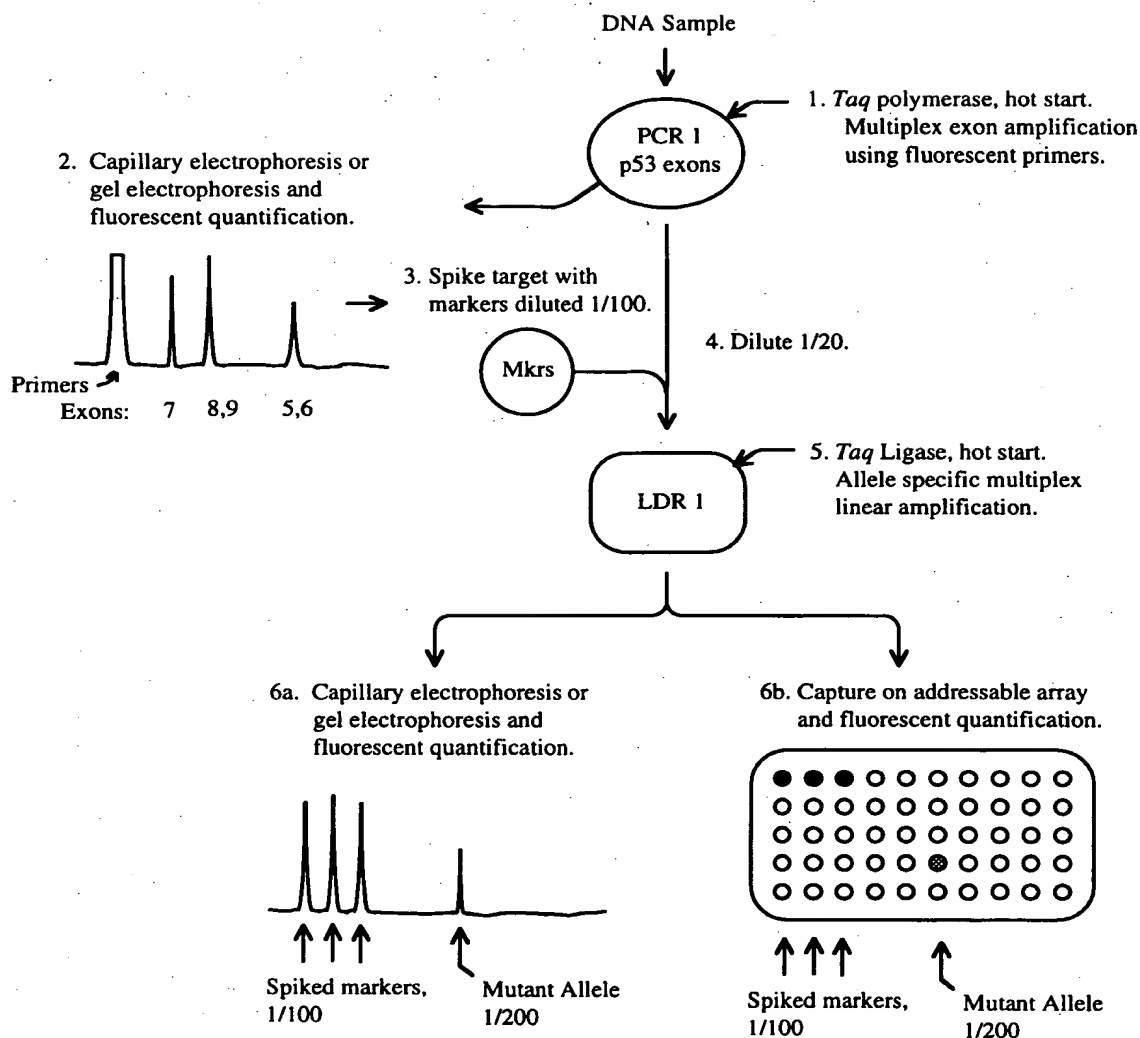
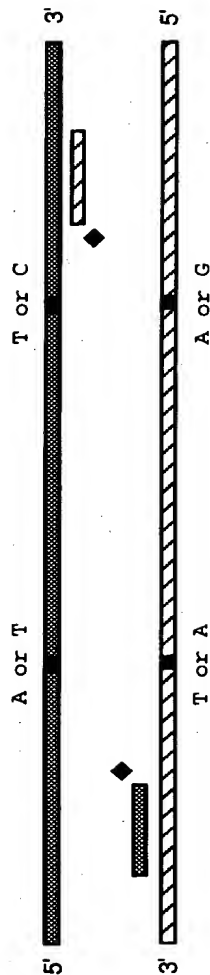


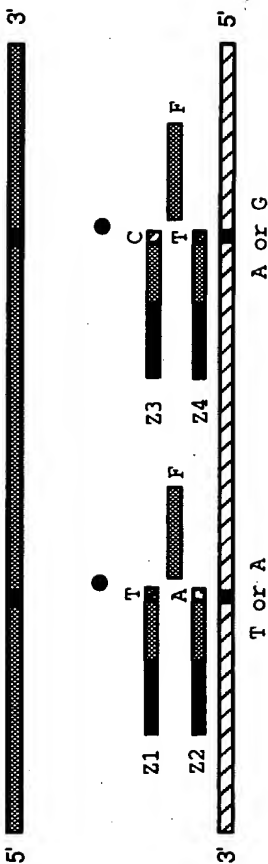
FIG. 2

PCR/LDR

1. PCR amplify region(s) containing mutations using primers, dNTPs and *Taq* polymerase. ♦



2. Perform LDR using allele-specific LDR primers and thermostable ligase. ●
 Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



3. Capture fluorescent products on addressable array and quantify each allele.

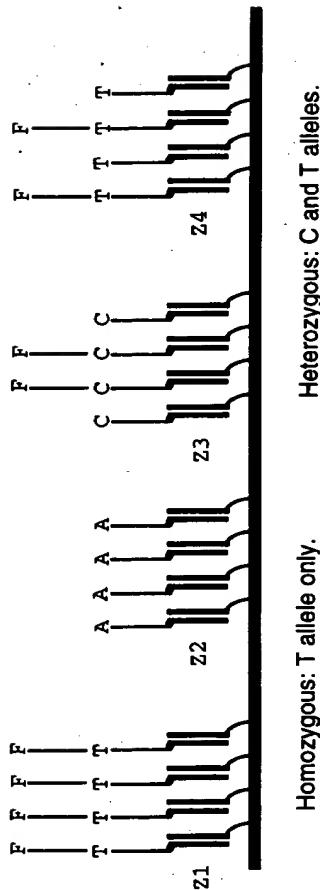
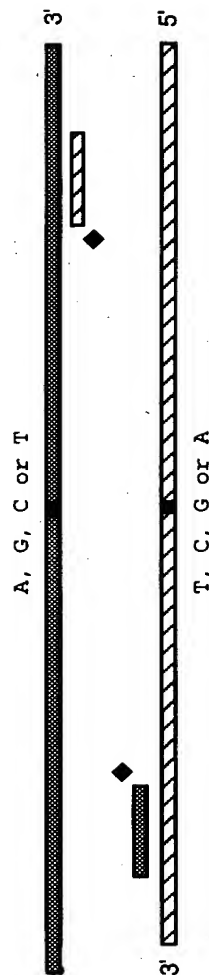


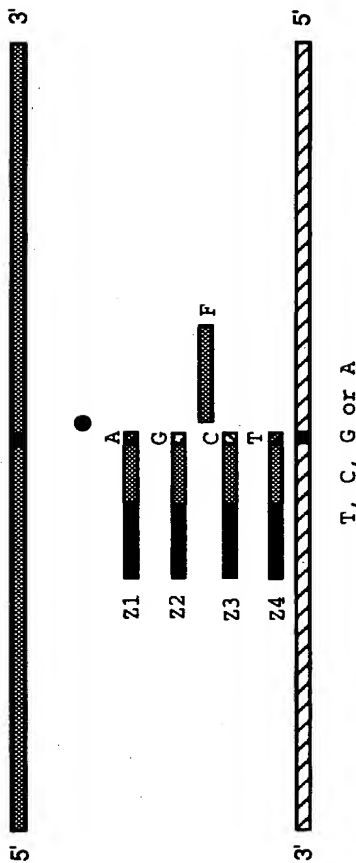
FIG. 3

PCR/LDR

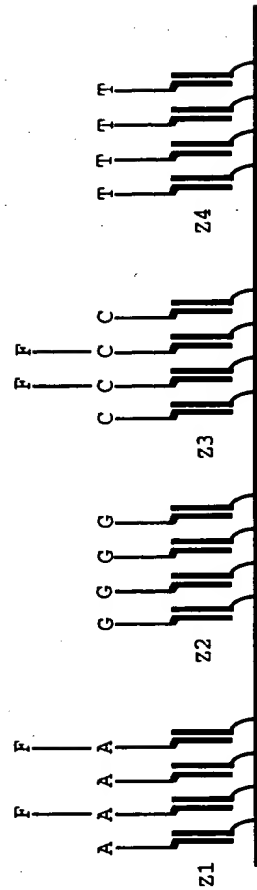
1. PCR amplify region(s) containing mutations using primers, dNTPs and Taq polymerase. ◆



2. Perform LDR using allele-specific LDR primers and thermostable ligase. ●
Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



3. Capture fluorescent products on addressable array and quantify each allele.

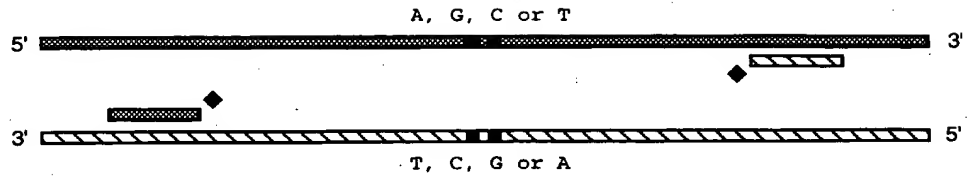


Heterozygous: A and C alleles.

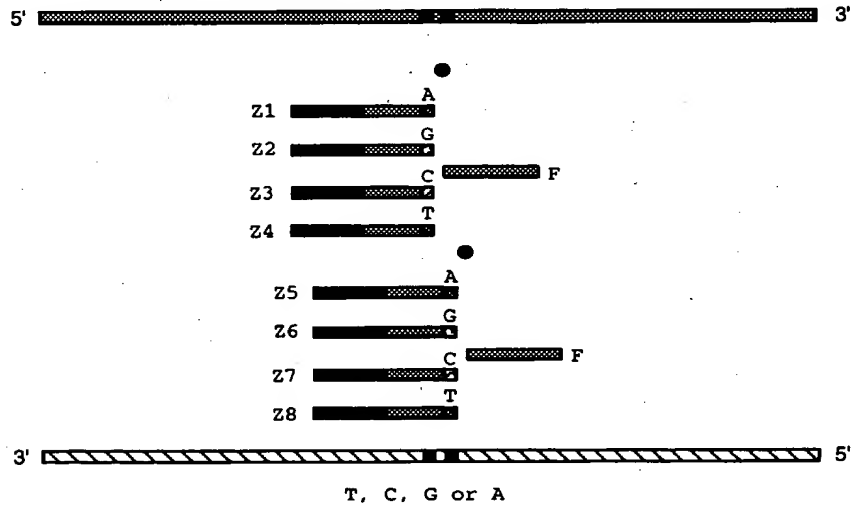
FIG. 4

PCR/ LDR : N arby alleles

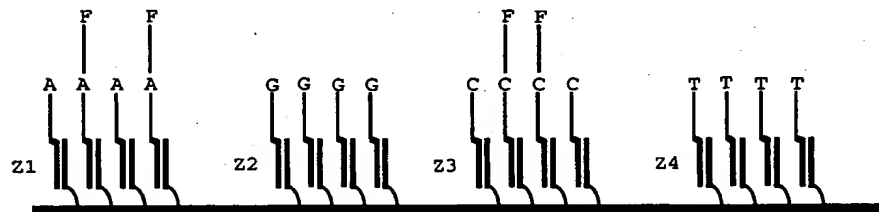
1. PCR amplify region(s) containing mutations using primers, dNTPs and *Taq* polymerase. ◆



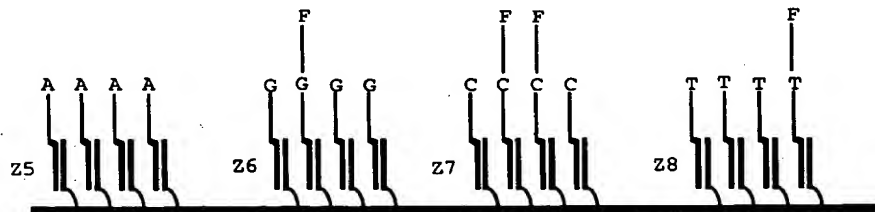
2. Perform LDR using allele-specific LDR primers and thermostable ligase. ●
 Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



3. Capture fluorescent products on addressable array and quantify each allele.



Heterozygous: A and C alleles.

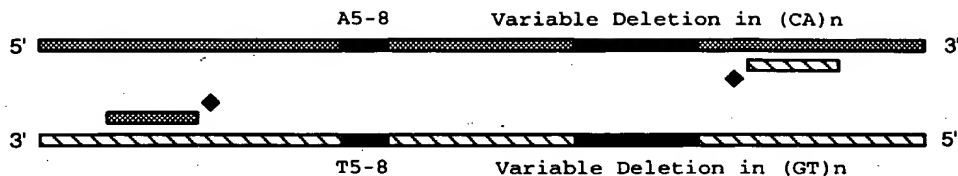


Heterozygous: G,C, and T alleles.

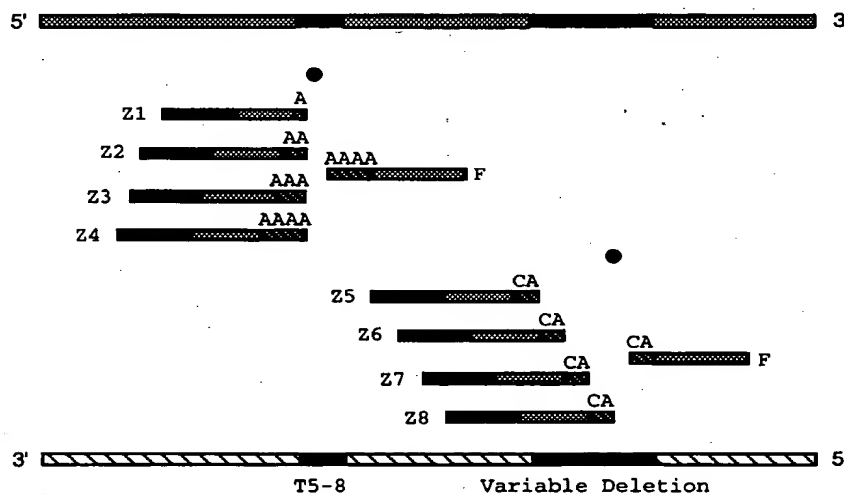
FIG. 5

PCR/ LDR : Insertions and Deletions

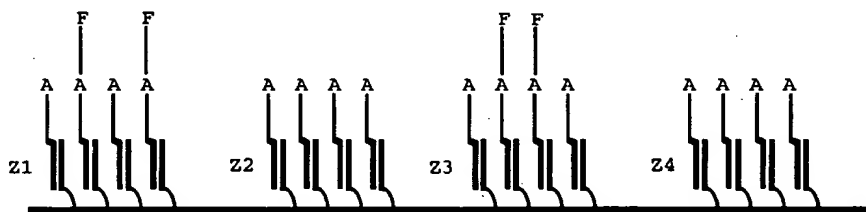
1. PCR amplify region(s) containing mutations using primers, dNTPs and *Taq* polymerase. ◆



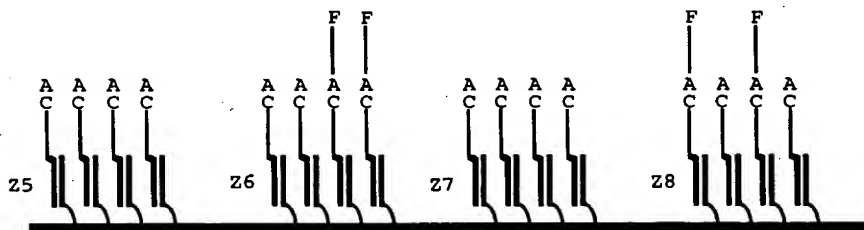
2. Perform LDR using allele-specific LDR primers and thermostable ligase. ●
Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



3. Capture fluorescent products on addressable array and quantify each allele.



Heterozygous: A5 and A7 alleles.



Heterozygous: (CA)5 and (CA)3 alleles.

FIG. 6

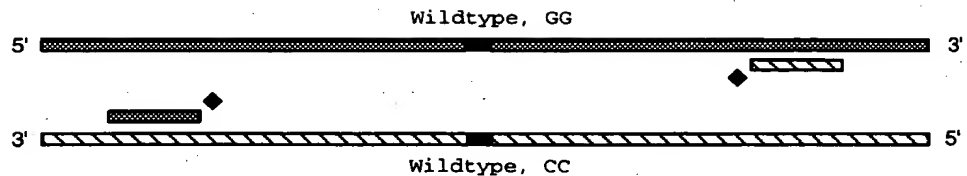


7/34

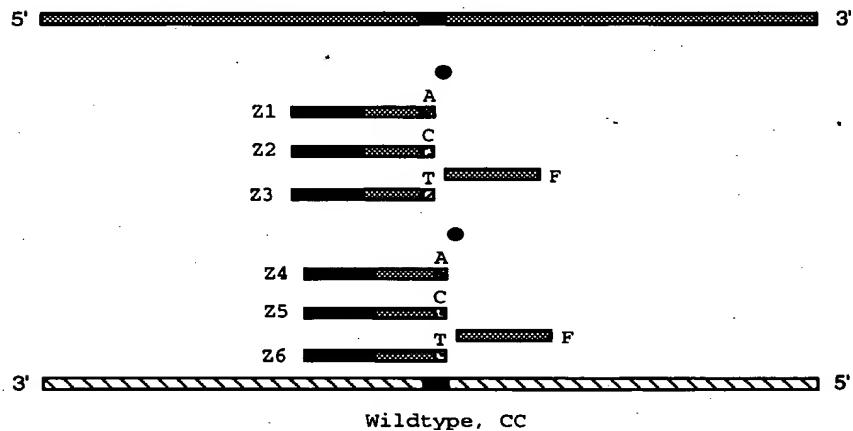
RECEIVED
FEB 14 2003
TECH CENTER 1600/2300

PCR/ LDR : Adjacent alleles, cancer detection

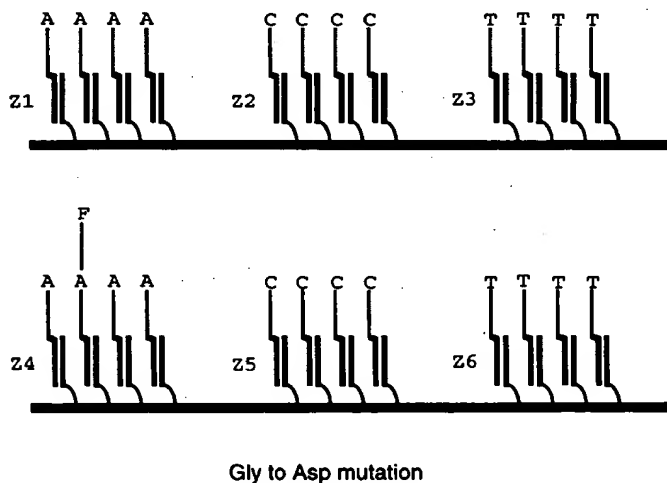
1. PCR amplify region(s) containing mutations using primers, dNTPs and *Taq* polymerase. ◆



2. Perform LDR using allele-specific LDR primers and thermostable ligase. ●
Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



3. Capture fluorescent products on addressable array and quantify each allele.

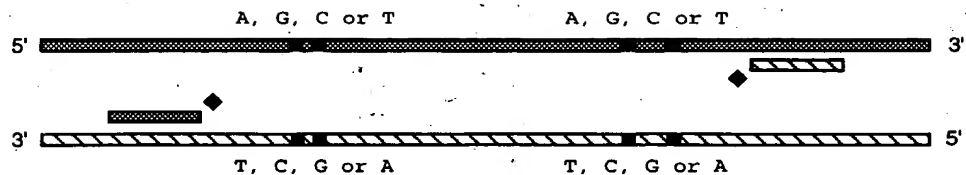


Gly to Asp mutation

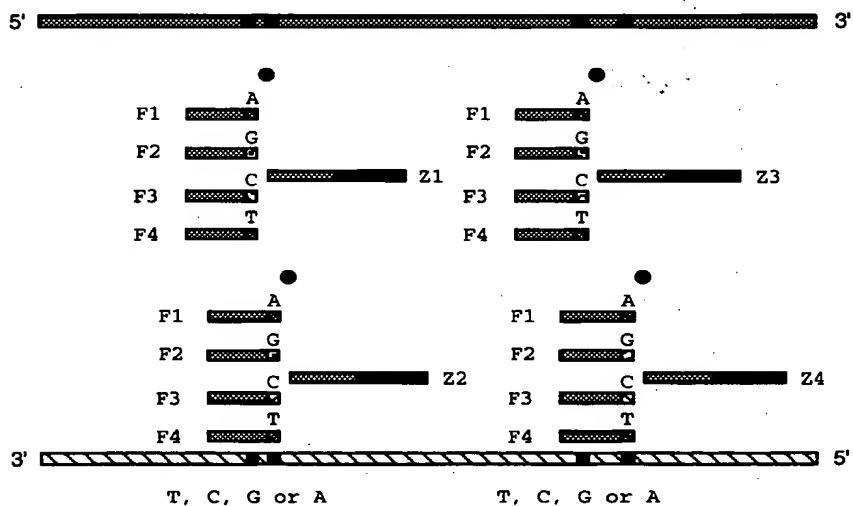
FIG. 7

PCR/ LDR : Nearby alleles

1. PCR amplify region(s) containing mutations using primers, dNTPs and *Taq* polymerase. ◆



2. Perform LDR using allele-specific LDR primers and thermostable ligase. ●
Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



3. Capture fluorescent products on addressable array and quantify each allele.

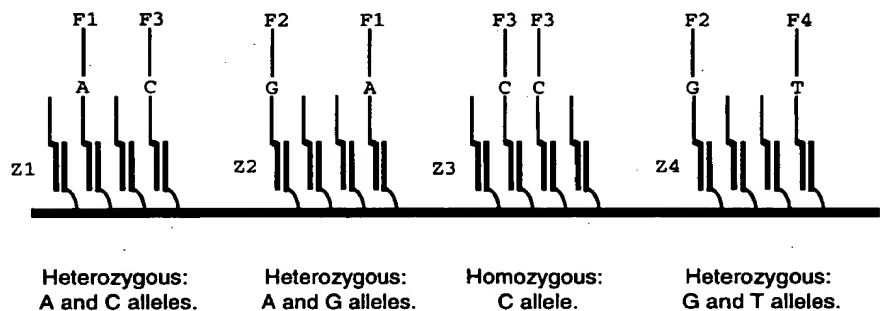
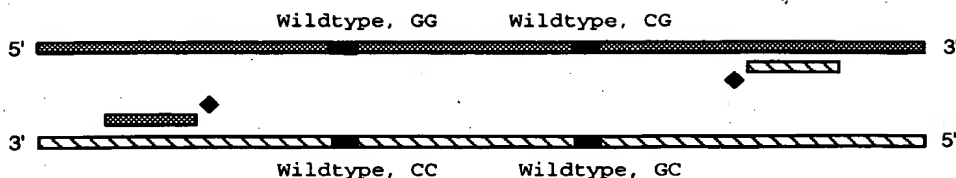


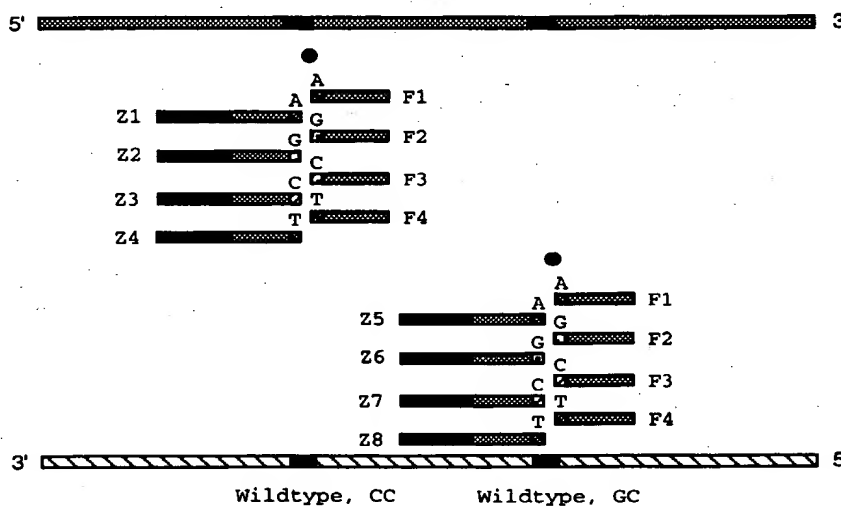
FIG. 8

PCR/ LDR : Adjacent and Nearby alleles

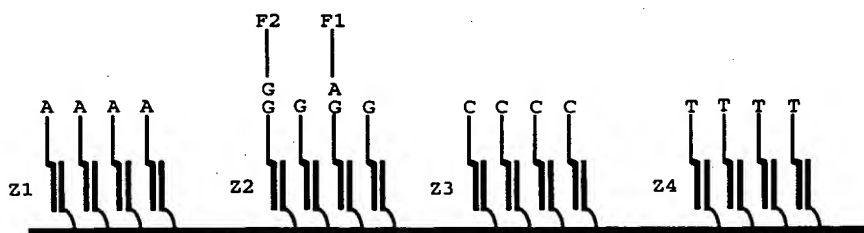
1. PCR amplify region(s) containing mutations using primers, dNTPs and Taq polymerase. ◆



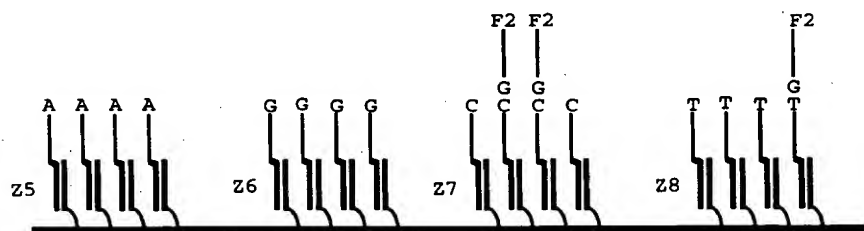
2. Perform LDR using allele-specific LDR primers and thermostable ligase. ●
Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



3. Capture fluorescent products on addressable array and quantify each allele.



Heterozygous: Gly and Glu alleles.

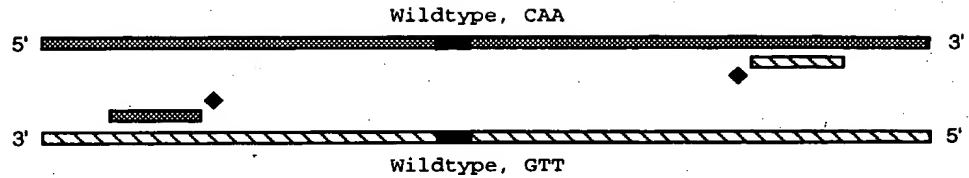


Het rozygous: Arg and Trp alleles.

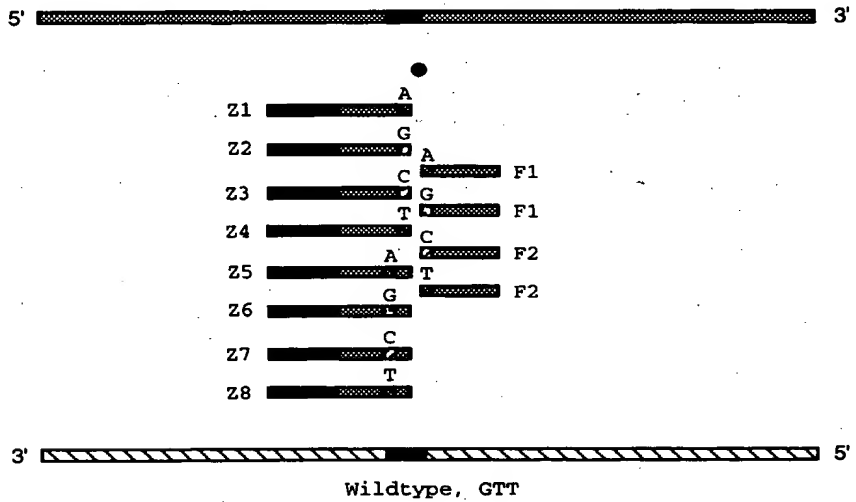
FIG. 9

PCR/ LDR : All alleles of a single codon

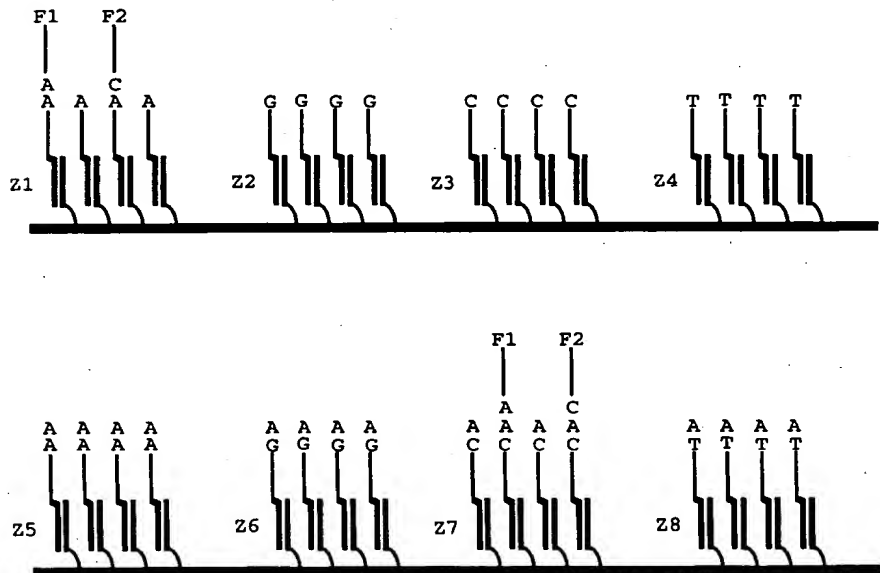
1. PCR amplify region(s) containing mutations using primers, dNTPs and *Taq* polymerase. ◆



2. Perform LDR using allele-specific LDR primers and thermostable ligase. ●
 Allele specific oligonucleotides ligate to common oligonucleotides only when there is perfect complementarity at the junction.



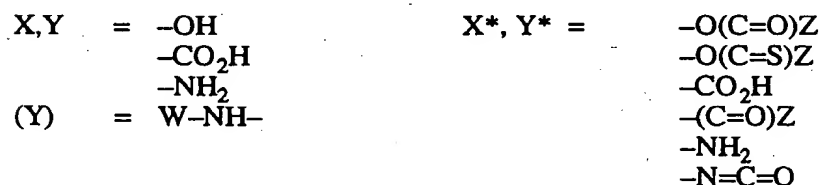
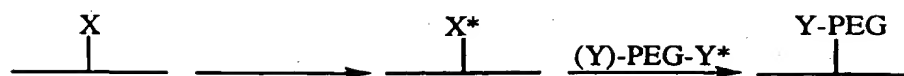
3. Capture fluorescent products on addressable array and quantify each allele.



Heterozygous: Gln and His alleles.

FIG. 10

RECEIVED
FEB 14 2003
TECH CENTER 1800/23



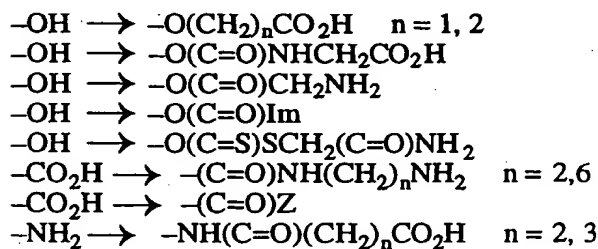
W = protecting group, e.g. Boc, Fmoc

Z = activating group, e.g. imidazole (Im), *p*-nitrophenol (OPnp),
hydroxysuccinimide (OSu), pentafluorophenol (OPfp)

PEG = oligo or poly(ethylene glycol), backbone $(\text{CH}_2\text{CH}_2\text{O})_n$ $n = 6$ to 200
(can also be grown by anionic polymerization with ∇)

WSC = water soluble carbodiimide

Functional group transformations/activation (as needed), $X \rightarrow X^*$, $Y \rightarrow Y^*$



Covalent linkage, $X^* + Y^*$

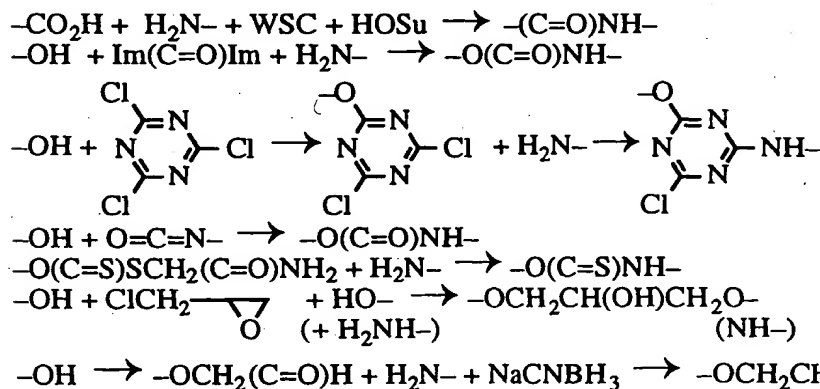
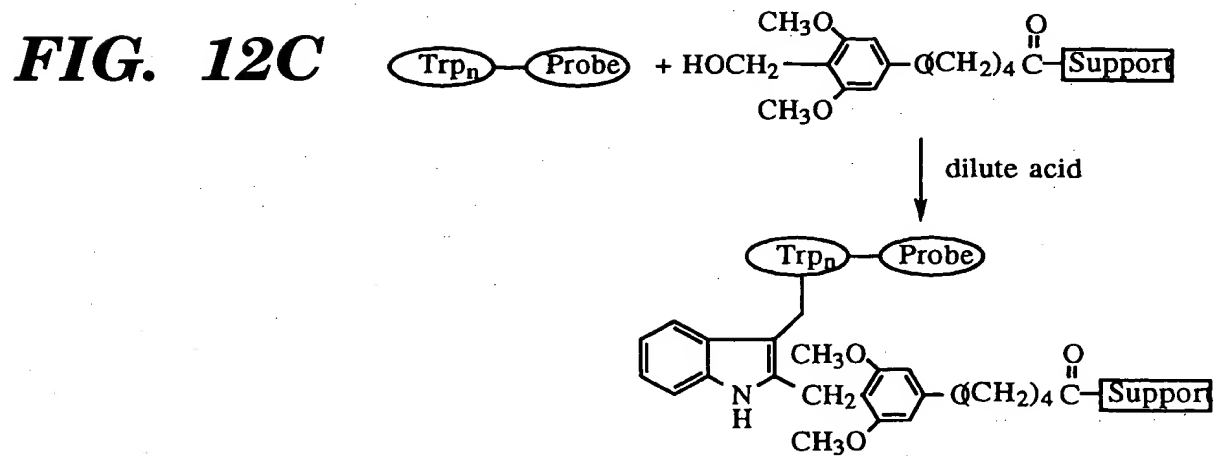
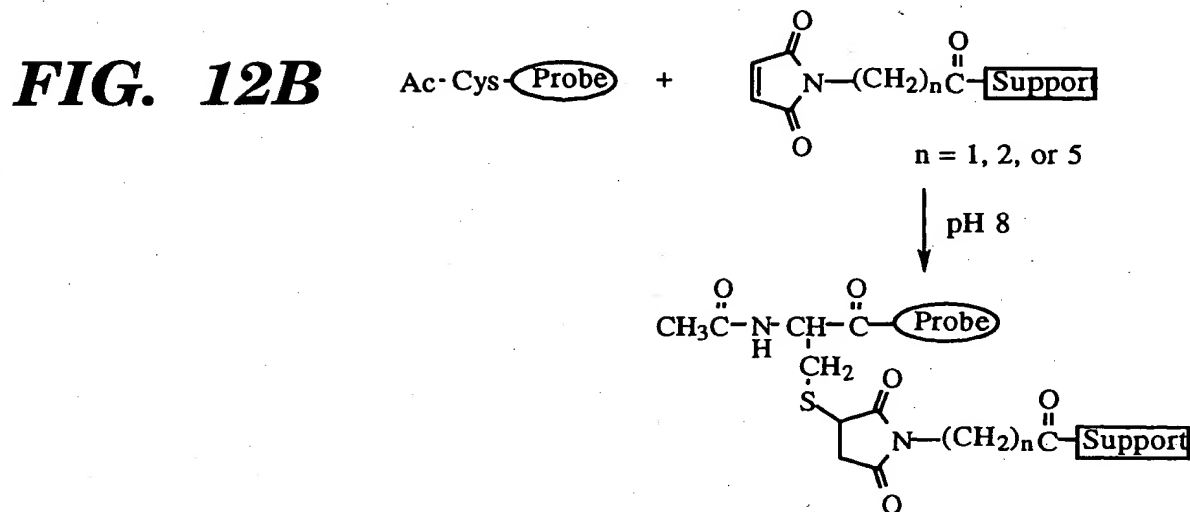
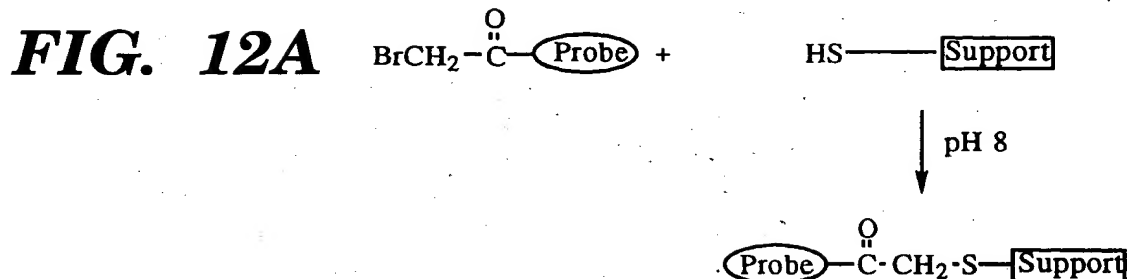


FIG. 11

12/34

RECEIVED
 FEB 14 2003
 TECH CENTER 16





13/34

RECEIVED
FEB 14 2003
TECH CENTER 1600/2000

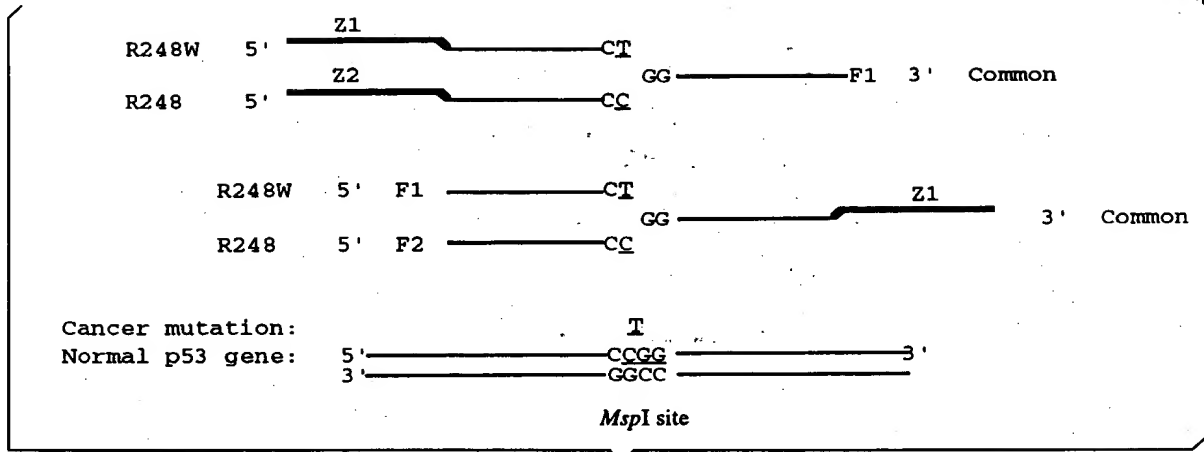


FIG. 13A

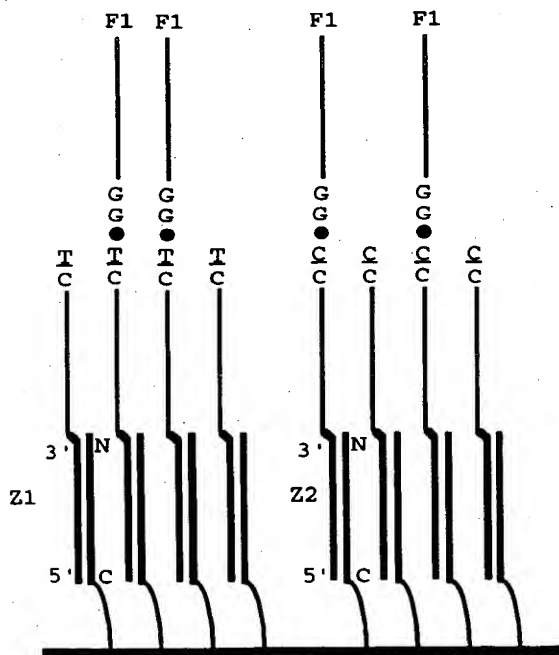


FIG. 13B

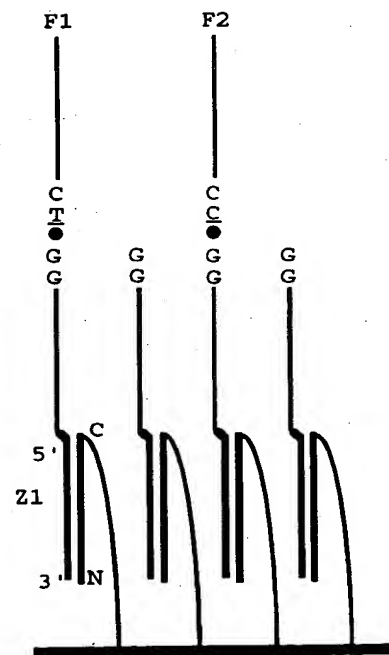


FIG. 13C



14/34

RECEIVED
FEB 14 2003
TECH CENTER 1600/2900

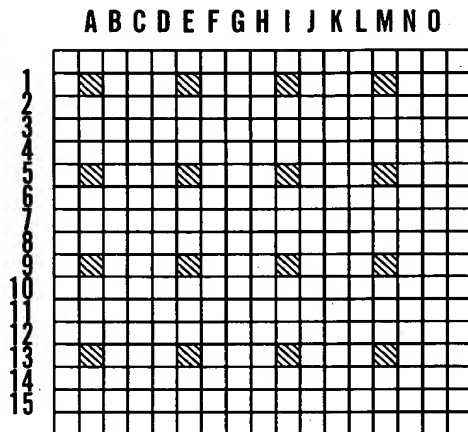


FIG. 14A

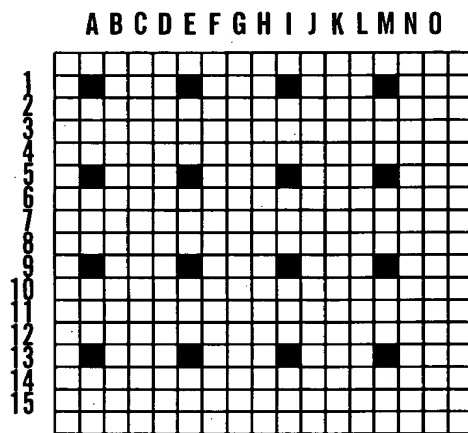


FIG. 14B

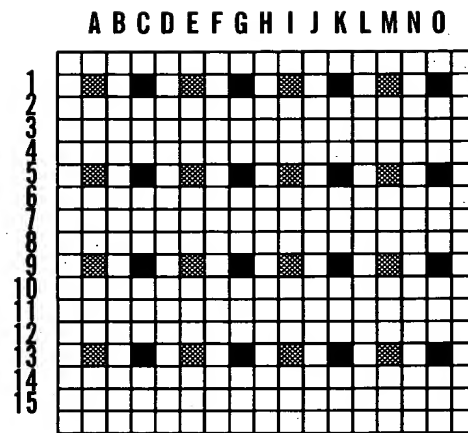


FIG. 14C

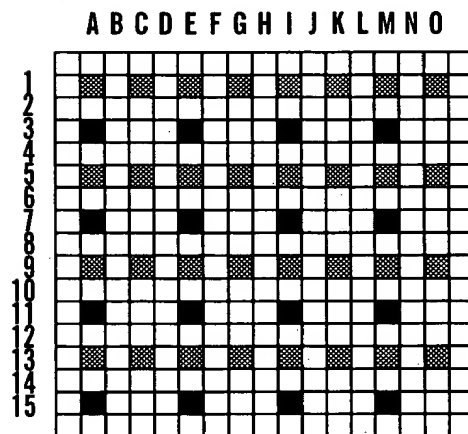


FIG. 14D

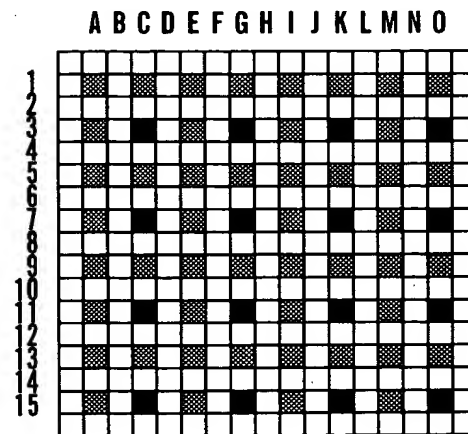


FIG. 14E

15/34

FIG. 15A

1st addition of unique 24mers.

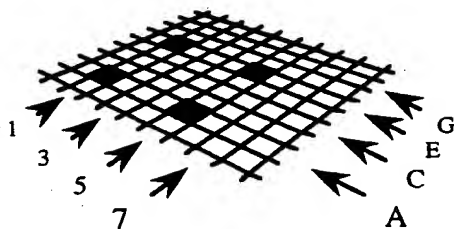


FIG. 15B

2nd addition of unique 24mers.

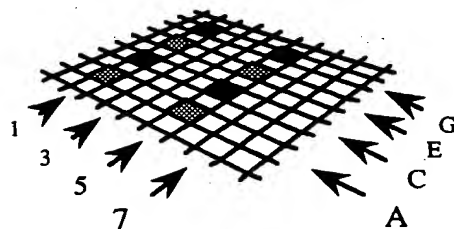


FIG. 15C

3rd addition of unique 24mers.

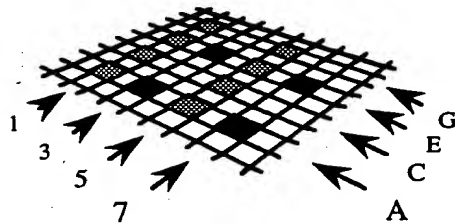


FIG. 15D

4th addition of unique 24mers.

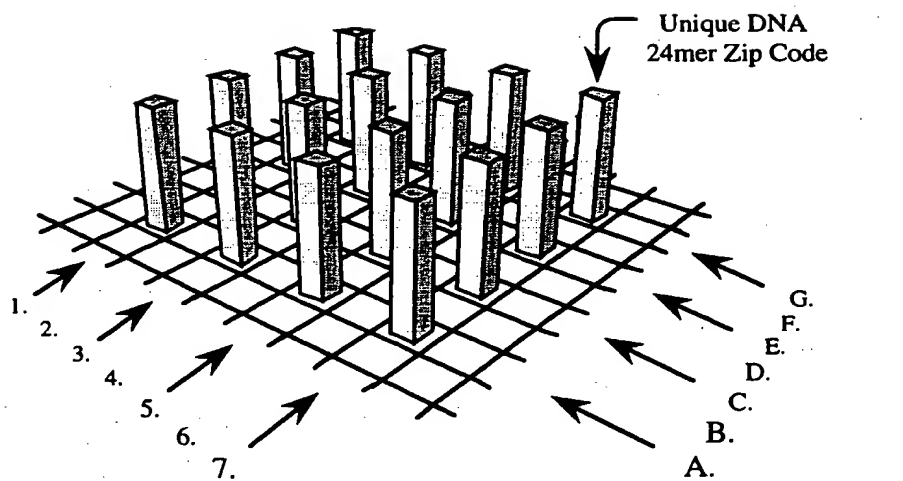
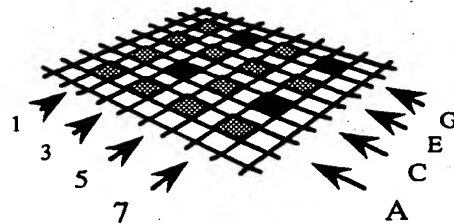


FIG. 15E

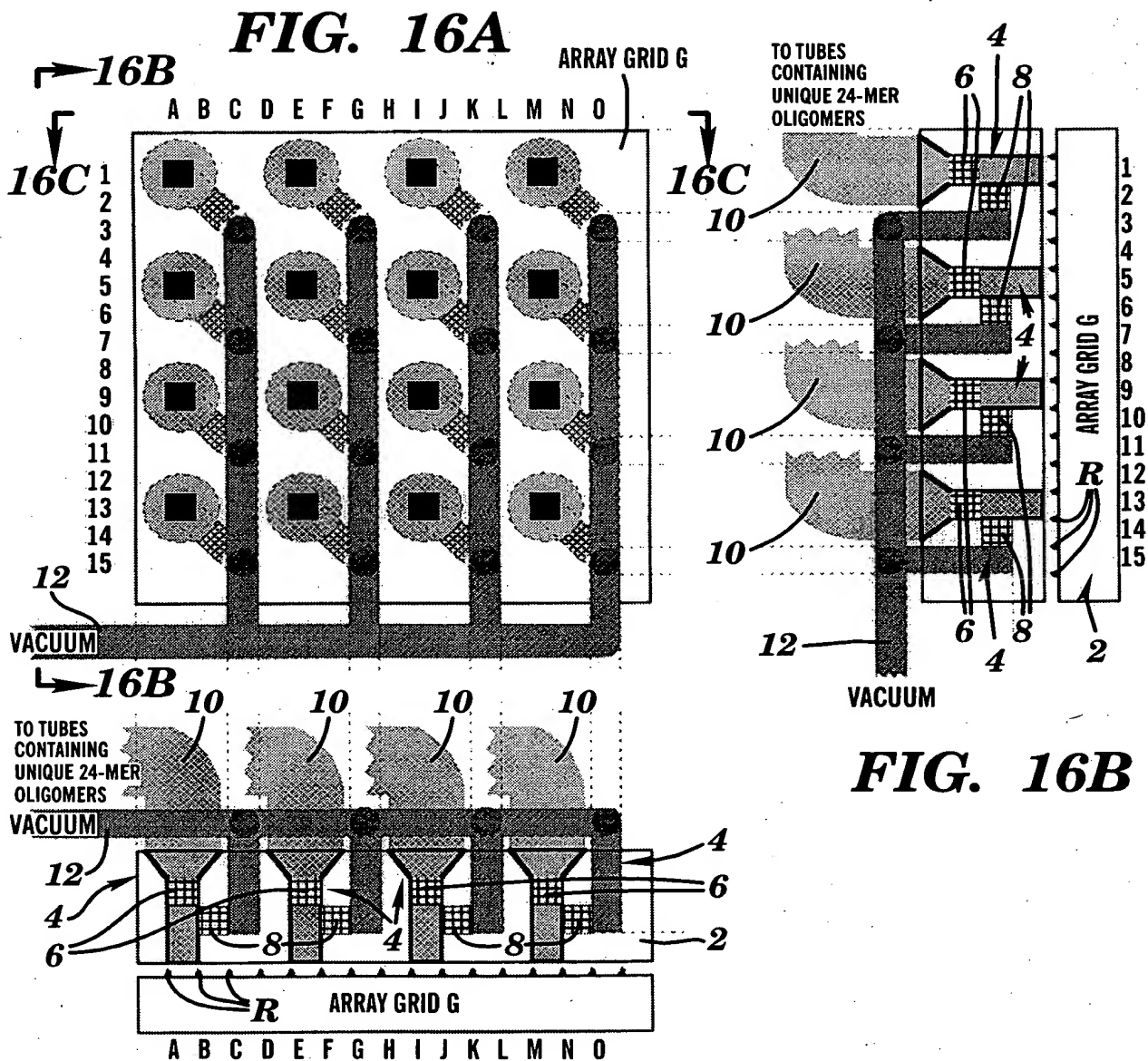


FIG. 16C

2ND TWO BASES

1ST TWO BASES

	TT	TC	TG	TA	CT	CC	CG	CA	GT	GC	GG	GA	AT	AC	AG	AA
TT							16'			23'		TTGA 6			TTAG 8	
TC			TCTG 1		30'	TCCC 3			TGCT 5							6'
TG		TGTC 2		36'			TCCG 4						TGAT 7		11'	
TA						18'		TACA 36			33'					
CT	32'		CTTG 9					CTCA 11	CTGT 13							8'
CC				CCTA 33					29'				CCAT 15			
CG	CGTT 10		12'					4'					28'			CGAA 16
CA		34'			25'		CAGC 12			CAGC 14		1'			9'	
GT					GTCT 19	24'				GTGC 22			31'			
GC	CGTT 17		14'											22'		GCAA 23
GG		20'		GGTA 18	35'							3'		GGAC 24		
GA			GATG 34			GACC 20		2'	GAGT 21							
AT						ATCG 28	7'				15'			ATAC 31		
AC		21'			ACCT 27					ACGG 29	5'				13'	
AG			AGTG 25			AGCC 35			27'			AGGA 30		19'		
AA		AATC 26					10'			17'					AAAG 32	

FIG. 17



1st Tetramer addition
(columns)

1	2	3	4	5
1	2	3	4	5
1	2	3	4	5
1	2	3	4	5
1	2	3	4	5

FIG. 18A

18/34

2nd Tetramer addition
(rows)

6	6	6	6	6
5	5	5	5	5
4	4	4	4	4
3	3	3	3	3
2	2	2	2	2

FIG. 18B

3rd Tetramer addition
(columns)

3	4	5	6	1
3	4	5	6	1
3	4	5	6	1
3	4	5	6	1
3	4	5	6	1

FIG. 18C

4th Tetramer addition
(rows)

2	2	2	2	2
1	1	1	1	1
6	6	6	6	6
5	5	5	5	5
4	4	4	4	4

FIG. 18D

5th Tetramer addition
(columns)

6	1	2	3	4
6	1	2	3	4
6	1	2	3	4
6	1	2	3	4
6	1	2	3	4

FIG. 18E

6th Tetramer addition
(rows)

3	3	3	3	3
2	2	2	2	2
1	1	1	1	1
6	6	6	6	6
5	5	5	5	5

FIG. 18F

Addressable array with full length PNA 24mers

1-6-3-2-6-3	2-6-4-2-1-3	3-6-5-2-2-3	4-6-6-2-3-3	5-6-1-2-4-3	
1-5-3-1-6-2	2-5-4-1-1-2	3-5-5-1-2-2	4-5-6-1-3-2	5-5-1-1-4-2	
1-4-3-6-6-1	2-4-4-6-1-1	3-4-5-6-2-1	4-4-6-6-3-1	5-4-1-6-4-1	
1-3-3-5-6-6	2-3-4-5-1-6	3-3-5-5-2-6	4-3-6-5-3-6	5-3-1-5-4-6	
1-2-3-4-6-5	2-2-4-4-1-5	3-2-5-4-2-5	4-2-6-4-3-5	5-2-1-4-4-5	

FIG. 18G

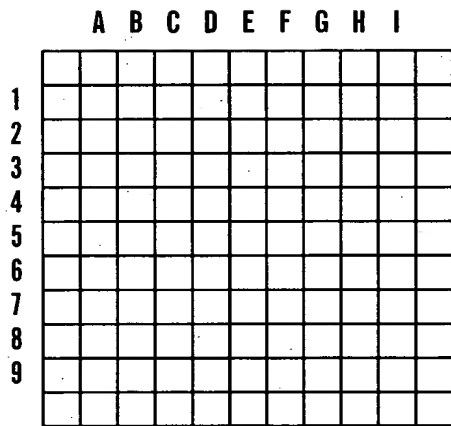


FIG. 19A

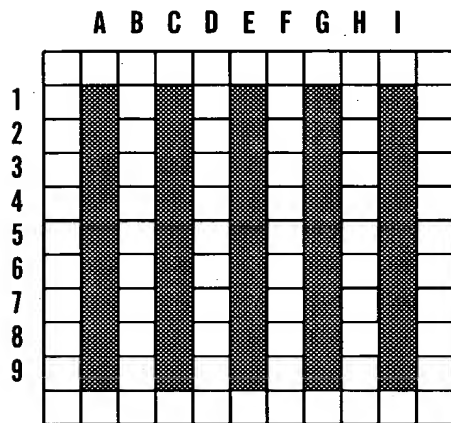


FIG. 19B

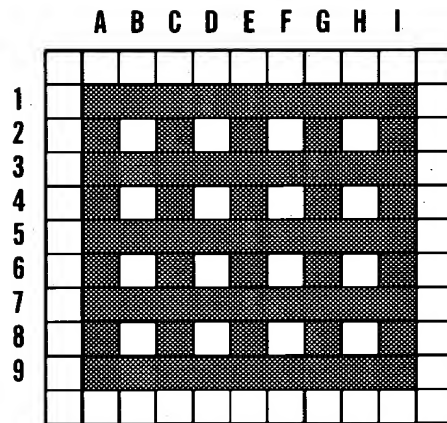


FIG. 19C

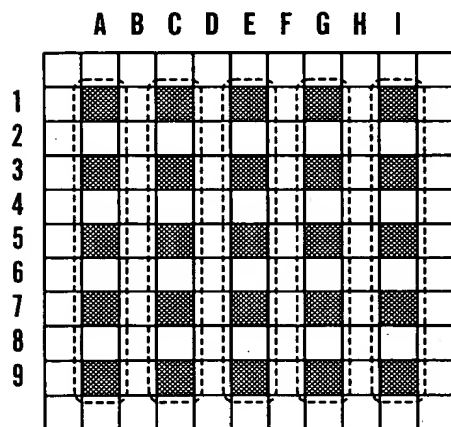


FIG. 19D

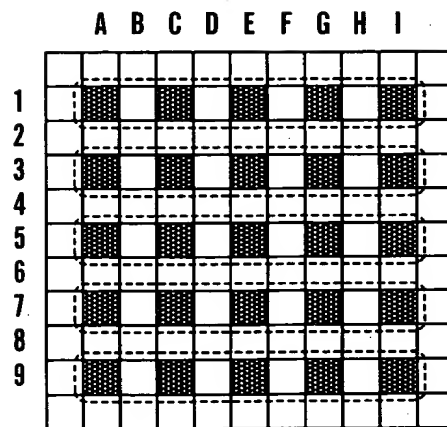


FIG. 19E

FIG. 20A

1st Tetramer additions
(columns)

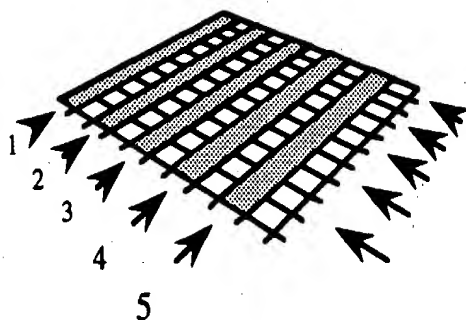


FIG. 20B

2nd Tetramer additions
(rows)

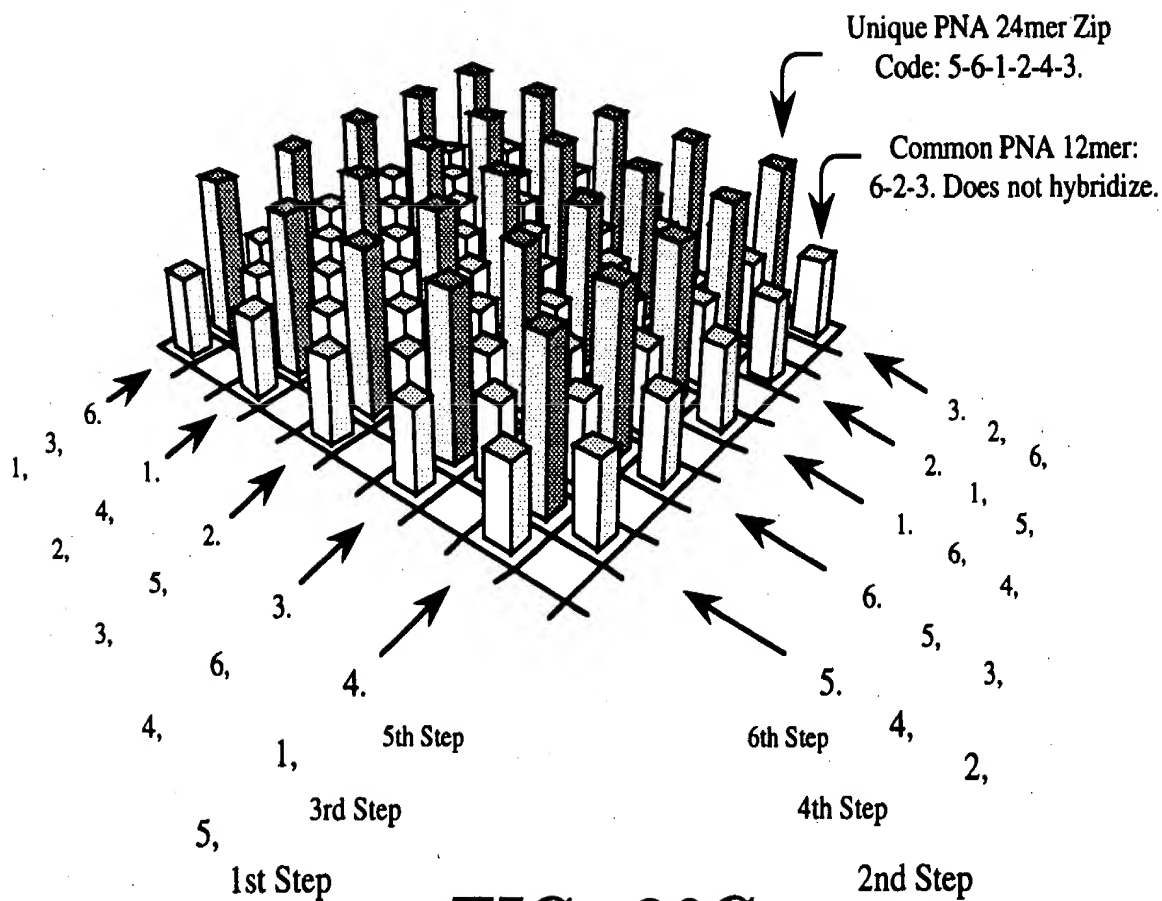
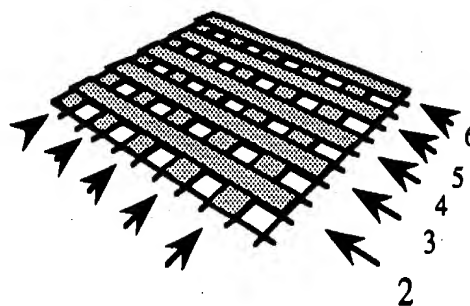


FIG. 20C

FIG. 21A



FIG. 21B

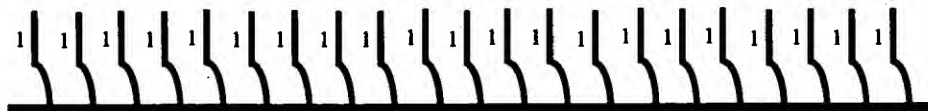


FIG. 21C

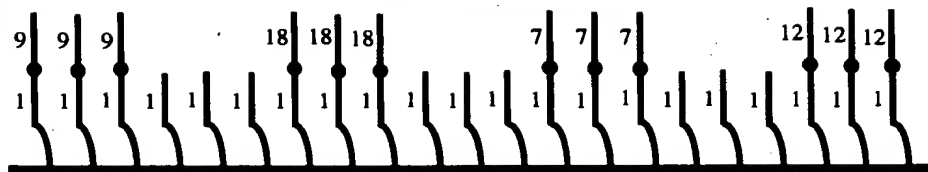


FIG. 21D

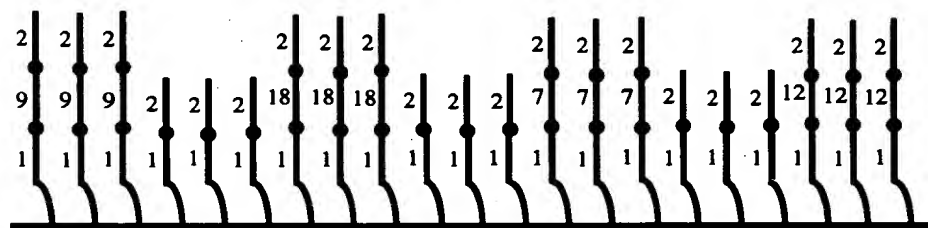


FIG. 21E

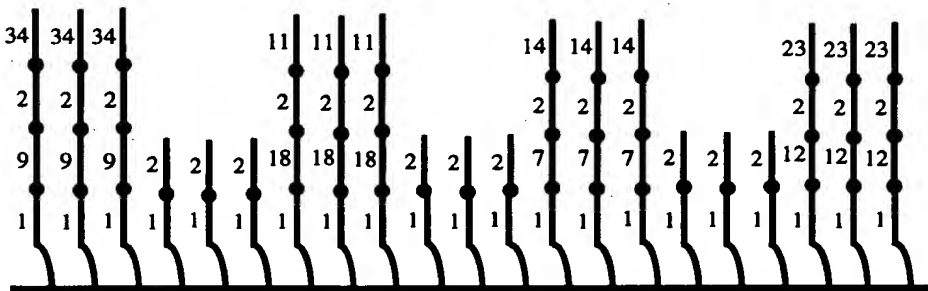


FIG. 21F

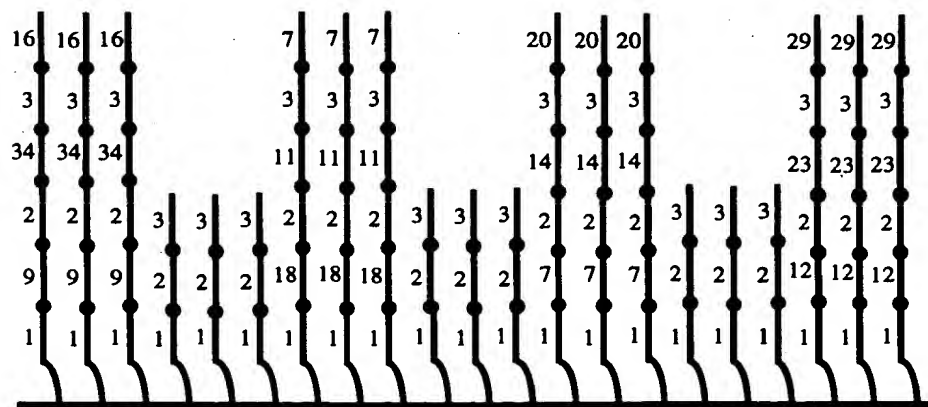


FIG. 22C



23/34

RECEIVED
FEB 14 2003
TECH CENTER 1800/2930

FIG. 23A

1st Tetramer additions
(columns)

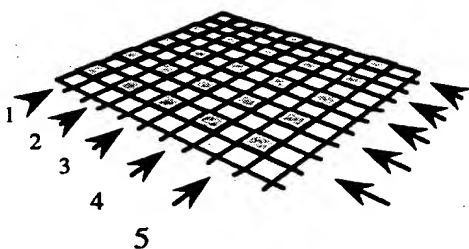


FIG. 23B

2nd Tetramer additions
(rows)

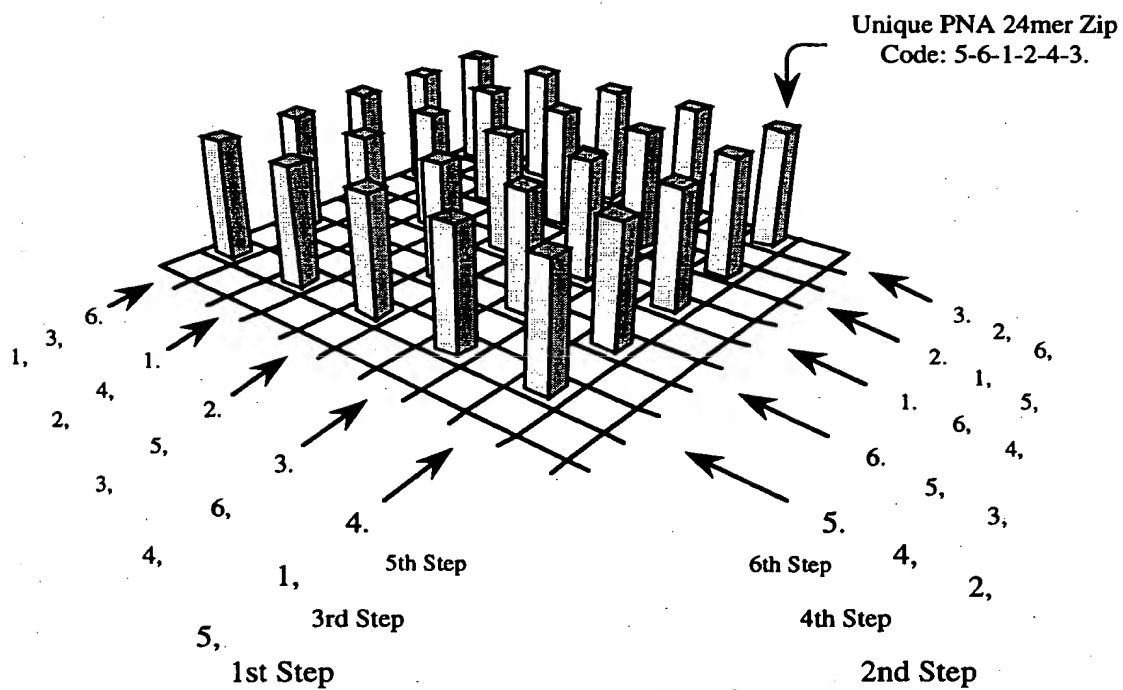
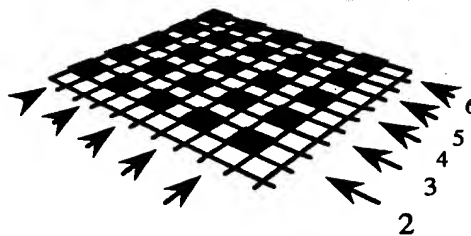


FIG. 23C

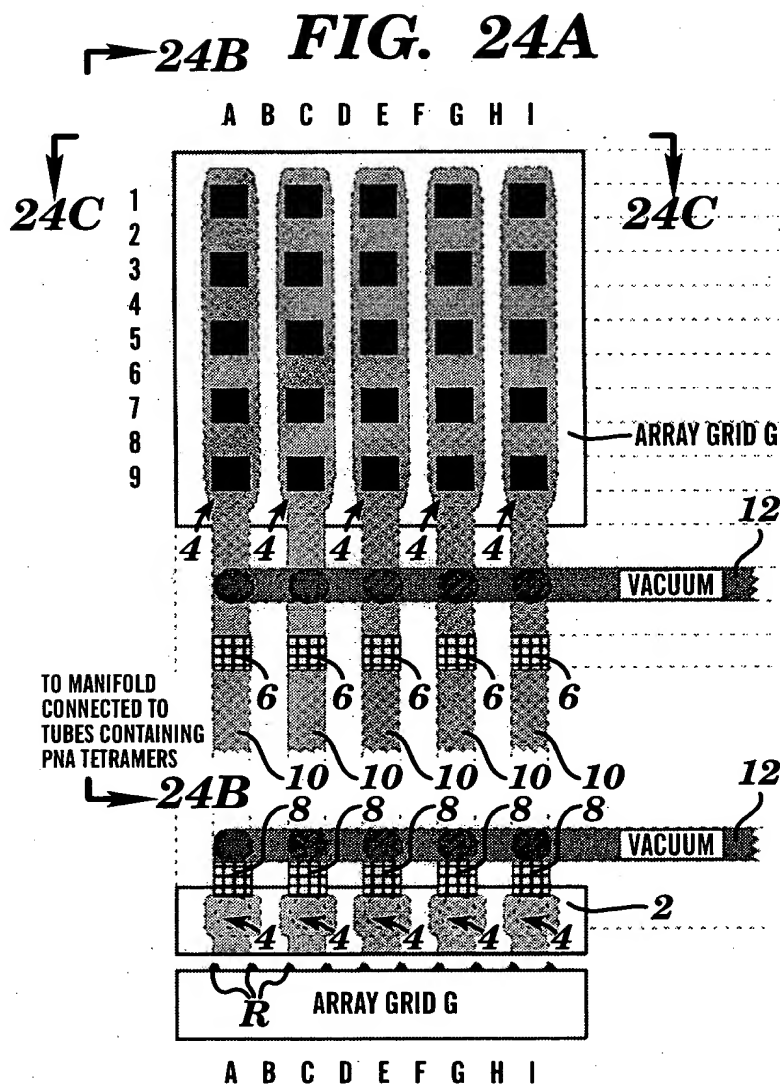


FIG. 24C

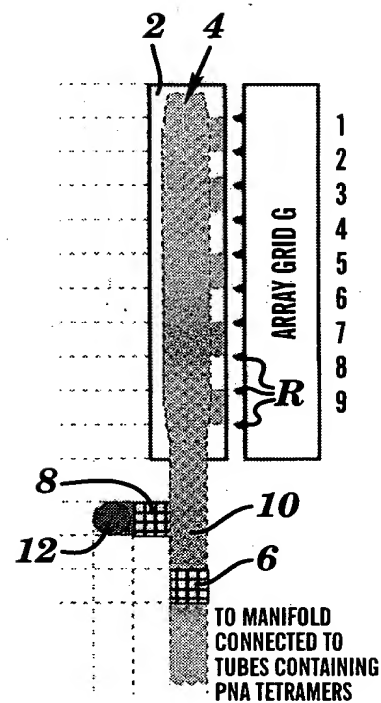


FIG. 24B



RECEIVED
FEB 14 2003
TECH CENTER 1600/2900

25/34

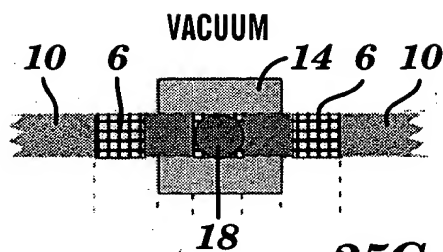


FIG. 25B

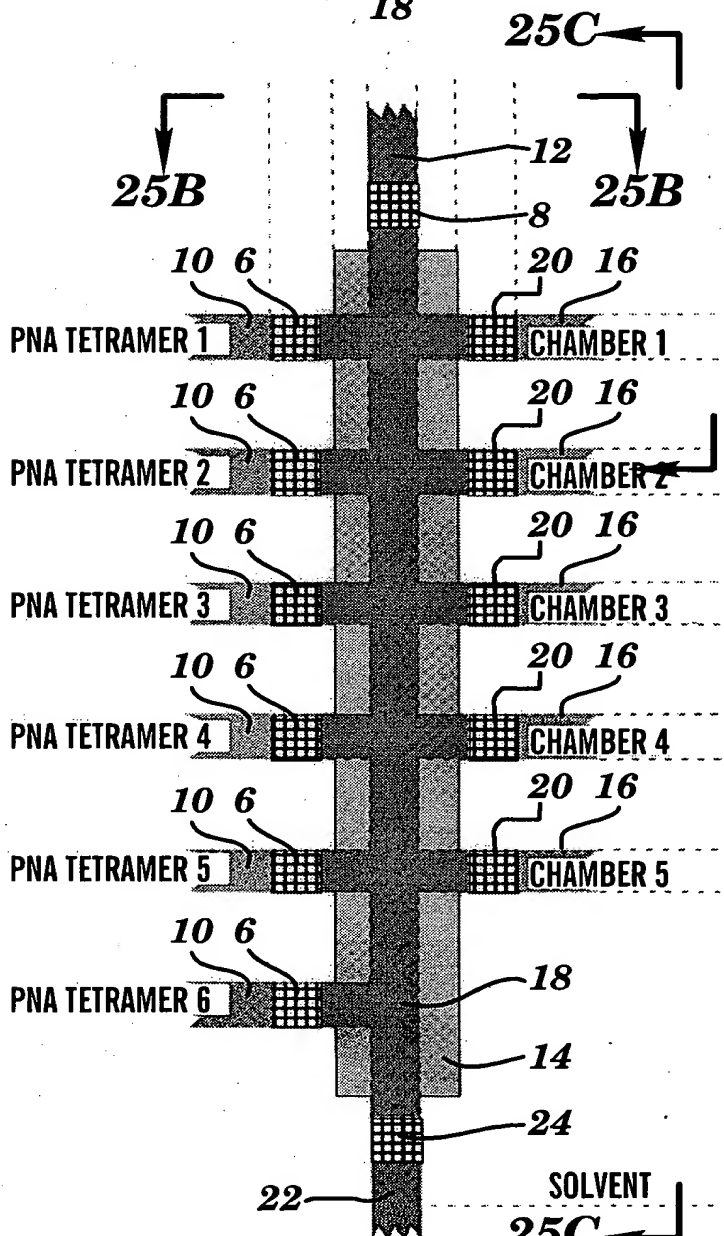


FIG. 25A

VALVE BLOCK
ASSEMBLY

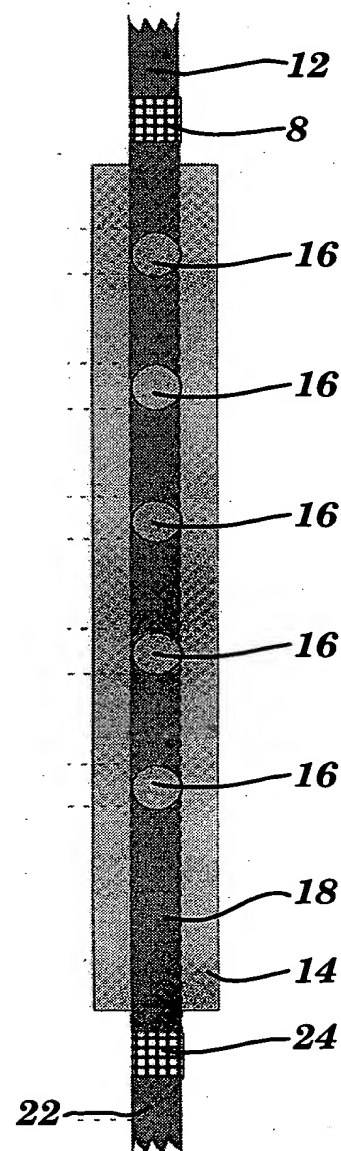


FIG. 25C

6 INPUTS AND 5 OUTPUTS



FIG. 26A 26/34

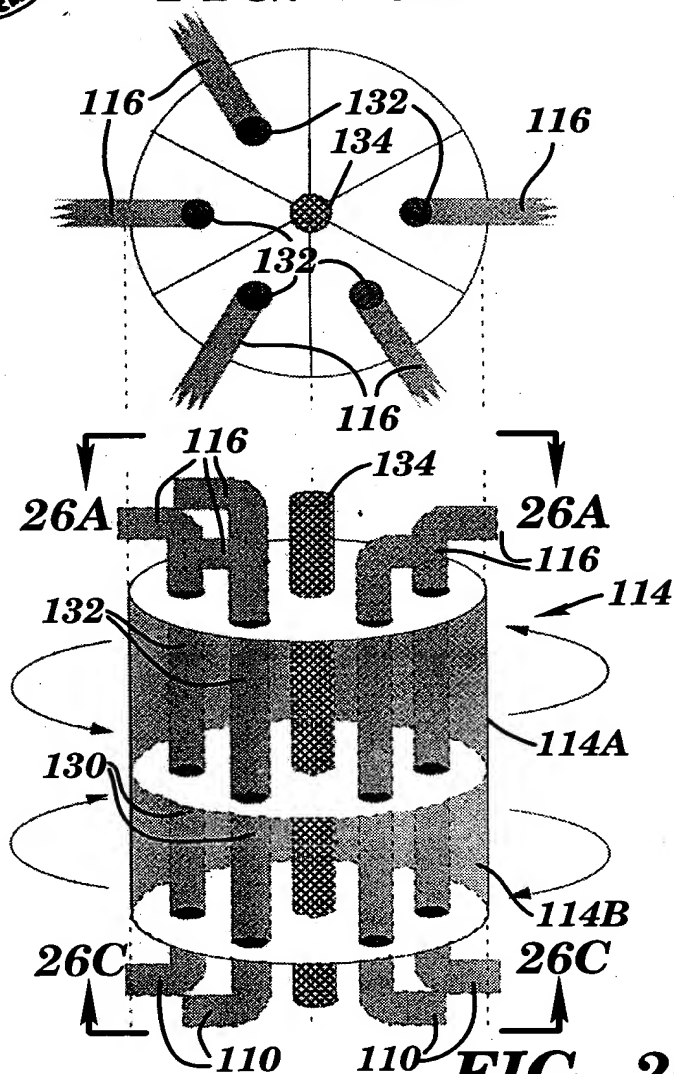


FIG. 26B

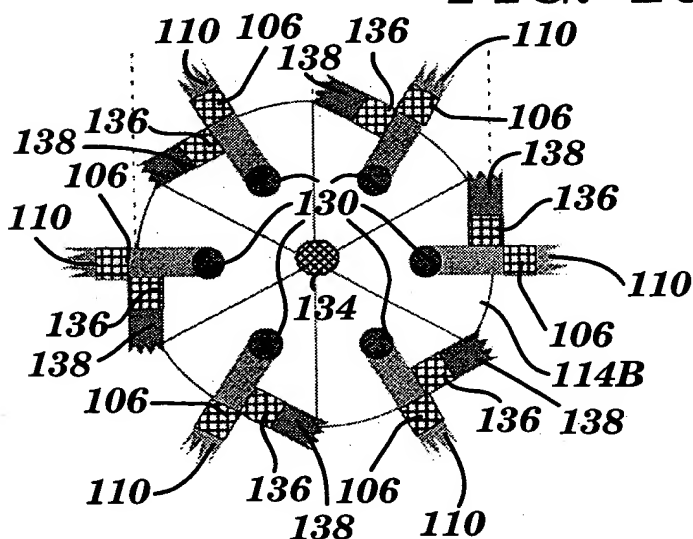


FIG. 26C

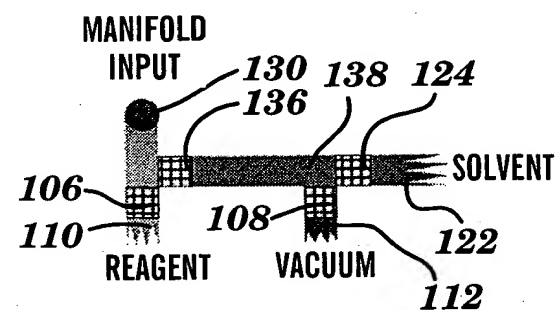
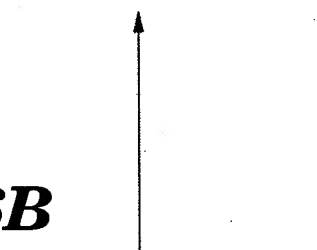
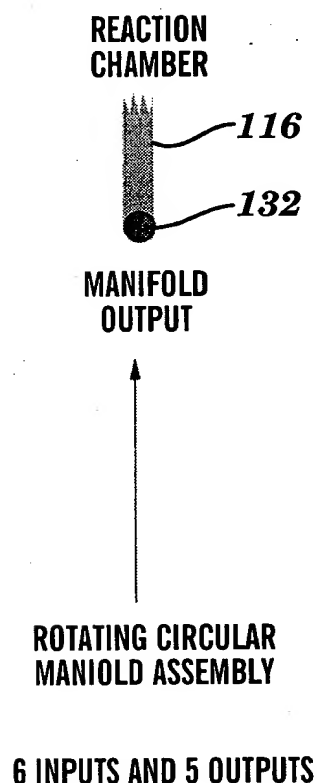


FIG. 26D



27/34

RECEIVED
FEB 14 2003
TECH CENTER 1600/2900

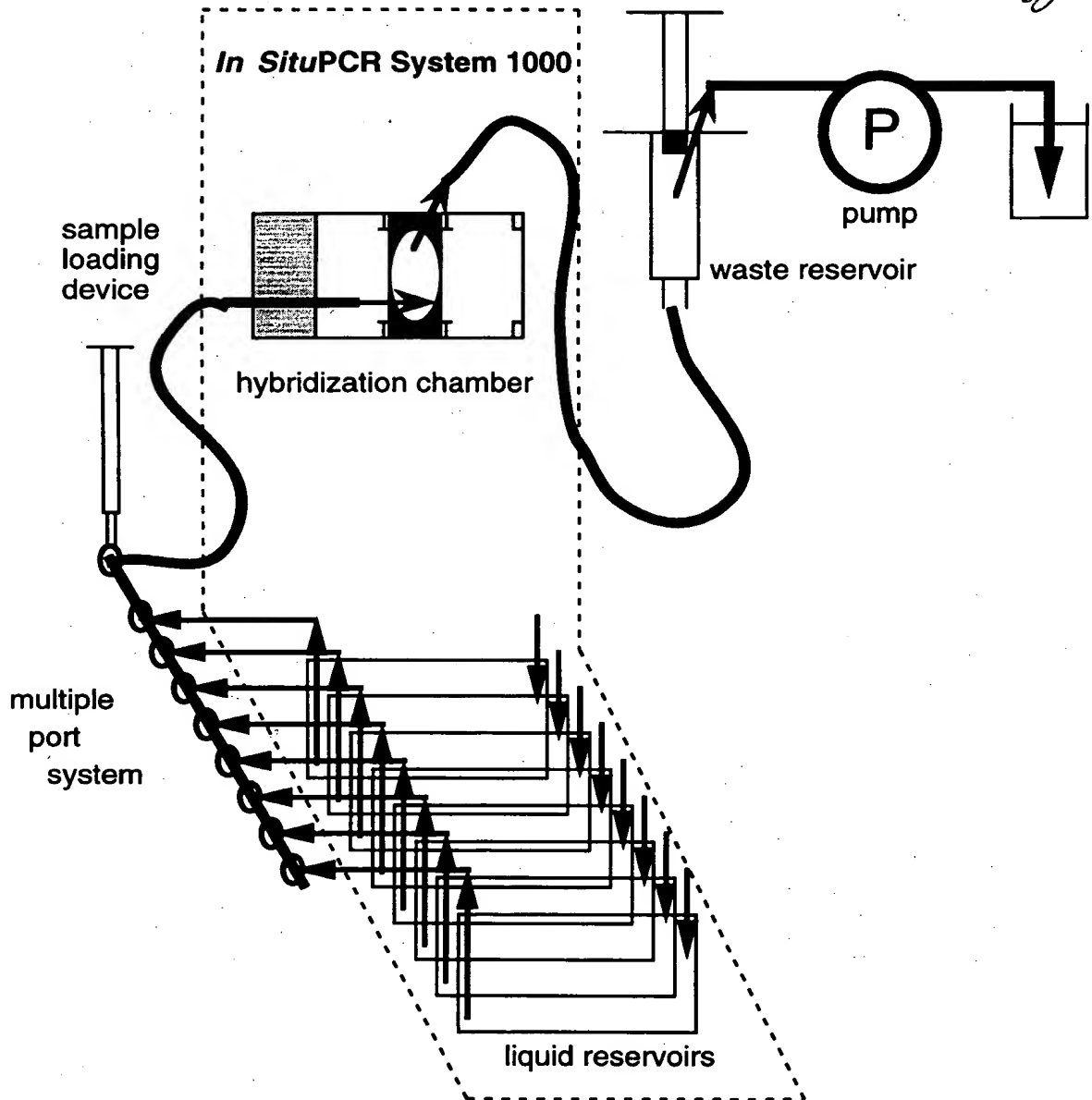


FIG. 27



28/34

RECEIVED
FEB 14 2003
TECH CENTER 1600/2900

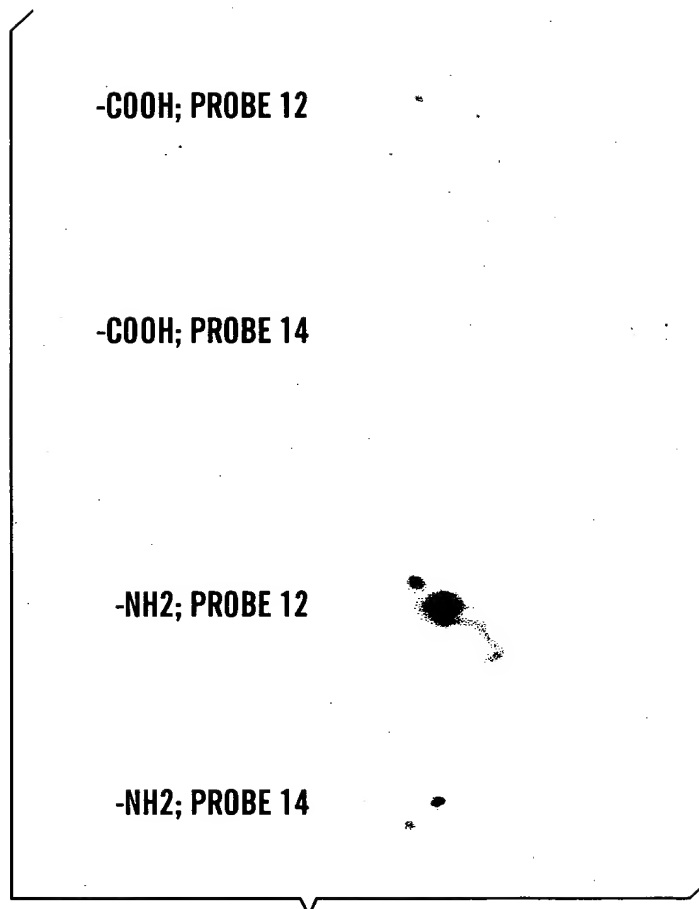


FIG. 28



29/34

RECEIVED
FEB 14 2003
TECH CENTER 1800/2900

2% EGDMA

2% HDDMA

4% EGDMA

FIG. 29



30/34

1 ●
2 ●

FIG. 30

31/34

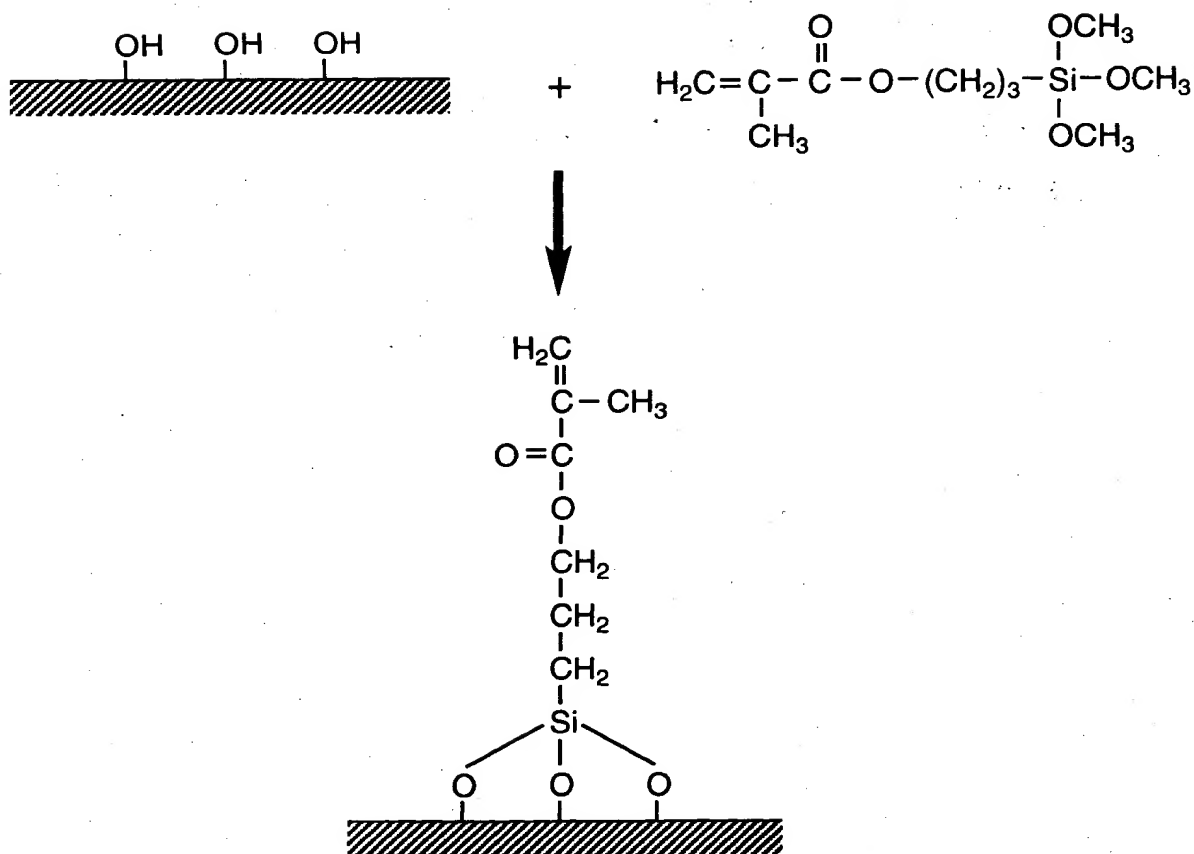


FIG. 31



32/34

RECEIVED
FEB 14 2003
TECH CENTER 1600/2900

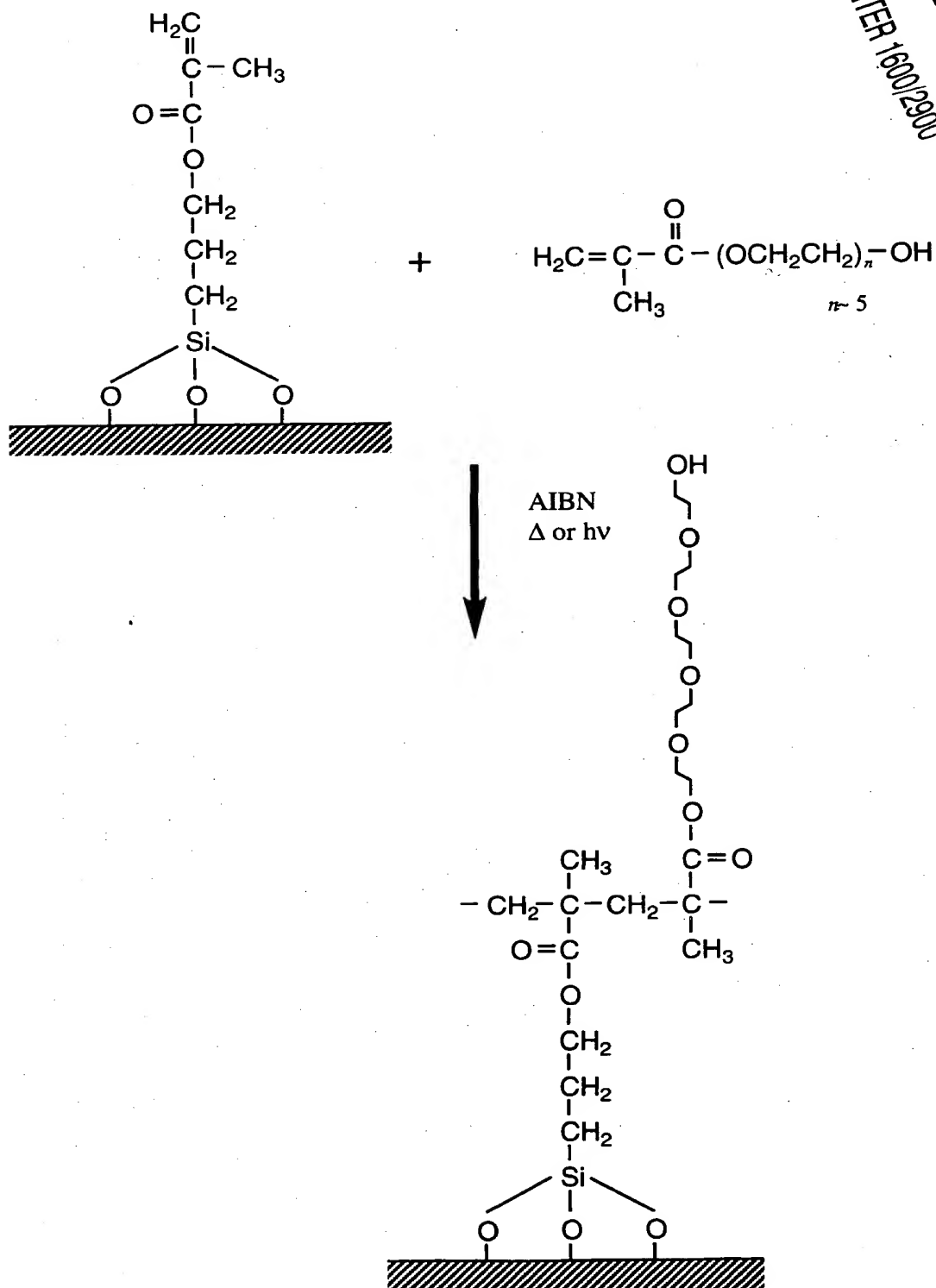


FIG. 32

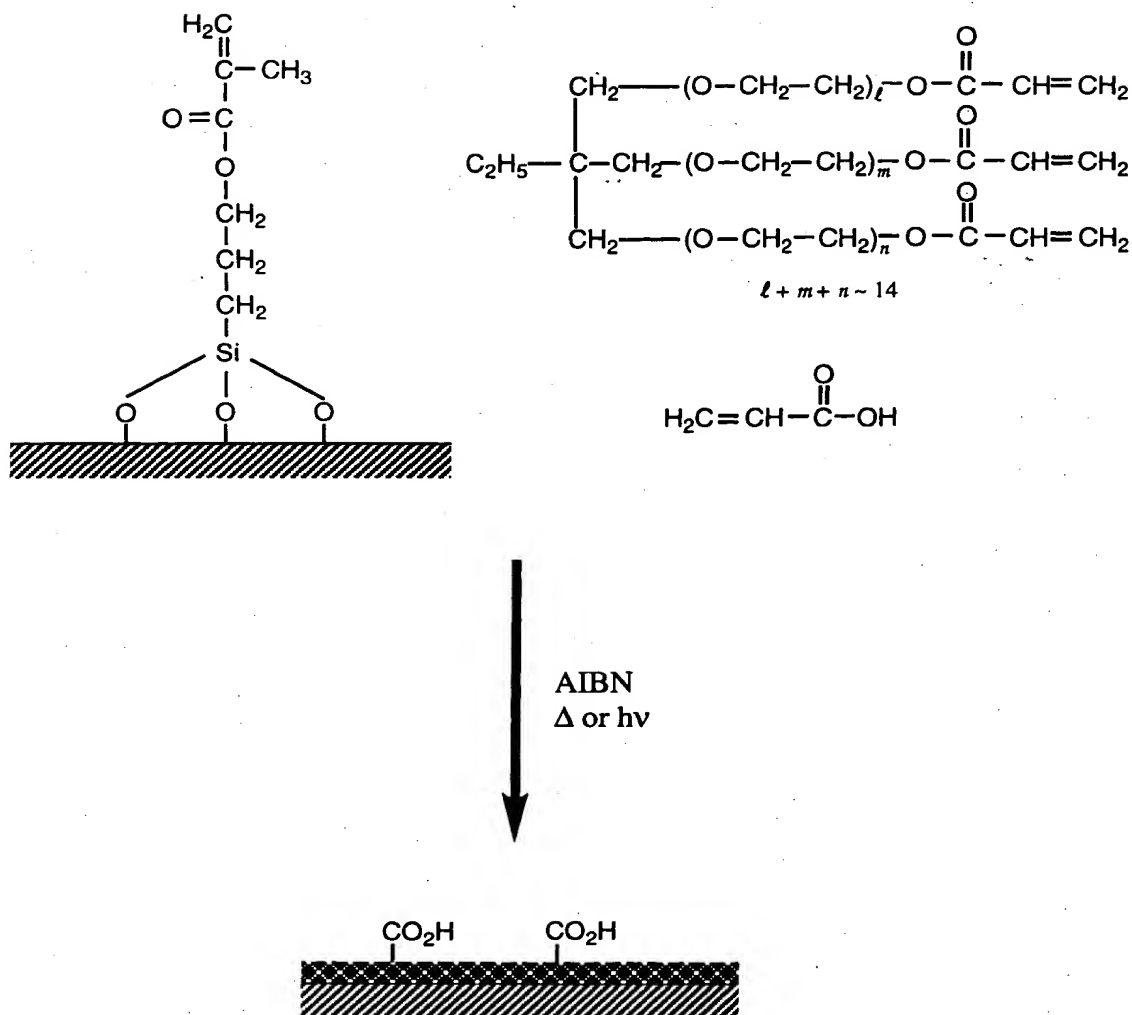


FIG. 33

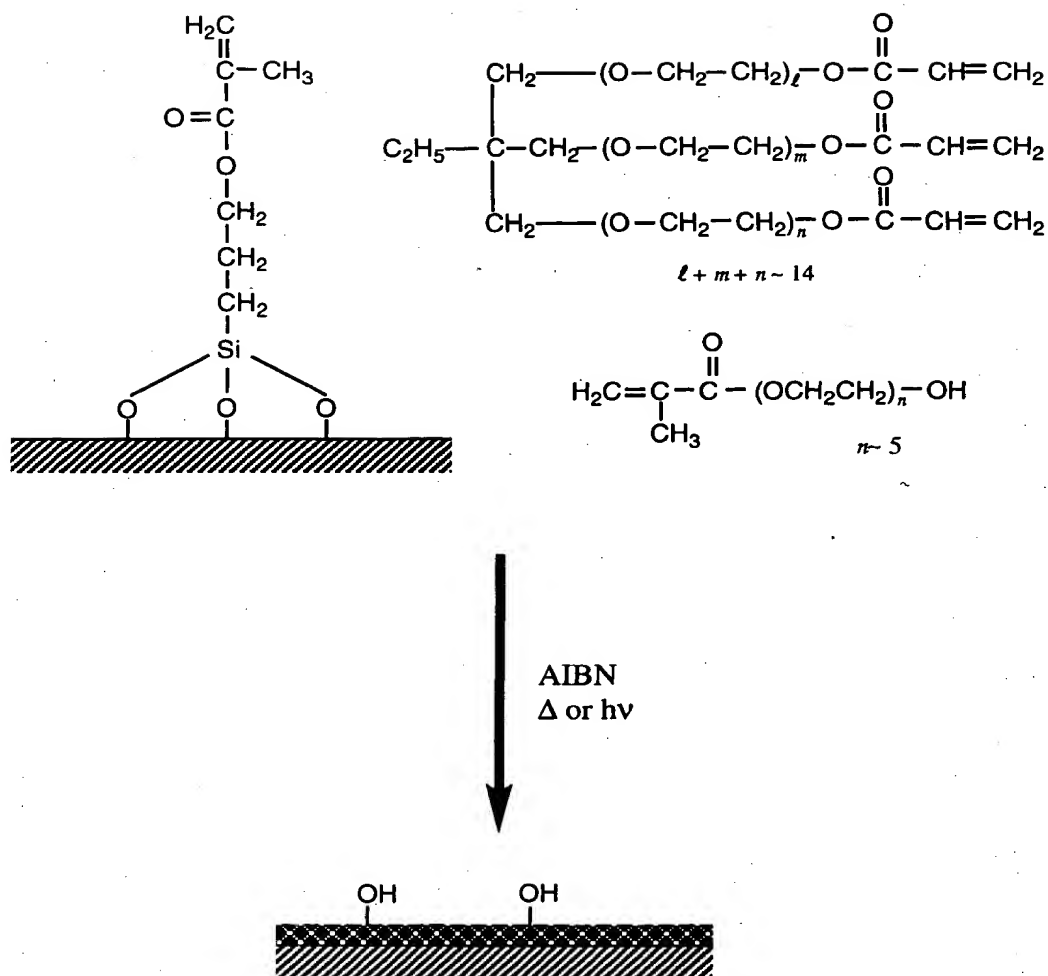


FIG. 34